Real-world implementation of the TRIANGLE regimen (without ASCT) in newly diagnosed mantle cell lymphoma: A multicenter analysis of effectiveness and safety

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INTRODUCTION & BACKGROUND

The landmark Phase III TRIANGLE trial redefined the frontline treatment of transplant-eligible mantle cell lymphoma (MCL) by demonstrating that adding ibrutinib to R-CHOP/R-DHAP induction and maintenance significantly improves outcomes.

However, the translation of these clinical trial results into routine daily clinical practice requires active real-world validation.

AIM & OBJECTIVES

We aimed to evaluate the effectiveness and safety of the TRIANGLE regimen in a real-world multicenter cohort of patients with newly diagnosed mantle cell lymphoma (MCL) outside of clinical trials.

METHODS

- **Study Design:** Retrospective, multicenter study across seven Spanish centers.
- **Cohort Size:** 27 patients with newly diagnosed MCL treated according to the no-ASCT TRIANGLE schema branch between 2024 and 2025.
- **Analyzed Variables:** Baseline clinic-biological variables, response rates evaluated according to Lugano criteria, and safety profile via CTCAE grade ≥3 adverse events (AEs).

CONCLUSIONS

Our data suggest that the TRIANGLE regimen is **highly effective and feasible** in real-world clinical practice, showing a safety profile consistent with clinical trials.

The high complete response rate and limited toxicity strongly support its frontline use.

Importantly, the zero-rate of ASCT in this series reflects a shifting paradigm toward ibrutinib-based consolidation in the "real world" setting.

RESULTS

Response Rates & Feasibility

- **Median Follow-up:** 12.2 months (range, 2.1–25.5) with 23 patients evaluable post-induction.
- **Post-induction Response:** 100% Overall Response Rate (ORR), with 87% Complete Response rate (CR; n=20), and 13% Partial Response rate (PR; n=3).
- **Treatment Transition:** 0% of patients proceeded to autologous stem cell transplantation (ASCT). 100% transitioned directly to ibrutinib-based maintenance (78% ibrutinib-rituximab).
- **Long-term Efficacy:** 100% overall survival to date; 22/23 patients (95%) maintain CR. Only 1 relapse occurred (high-risk features: blastoid variant, *TP53* mutation, Ki-67 >30%).

Safety Profile (Bimodal Toxicity)

- **Induction Phase (n=27):** Ibrutinib delays/interruptions occurred in 14% of patients (primarily grade ≥3 neutropenia (11.1%) and bleeding (3.7%)). **0%** definitive discontinuations. Most frequent AEs: infections (29%) and grade ≥3 neutropenia (25%).
- **Maintenance Phase (n=23):** 17.4% required dose reductions (to 420 mg) and 17.4% required temporary interruptions (due to gastrointestinal toxicity, bleeding, or infections). Only 1 patient (4.3%) discontinued treatment definitively (due to disease progression).
- **Maintenance AEs:** Shift towards chronic toxicity; most frequent were hypertension (13%), bleeding (13%), and infections (13%).

Baseline Characteristic	Result (N=27)
Demographics and General Status	
Age in years, median (range)	**60 (43 - 74)**
Male sex, n (%)	**20 (74.1%)**
ECOG Performance Status 0 - 1 / ≥2	**26 (96.3%) / 1 (3.7%)**
Clinical Stage and Prognostic Indexes	
Advanced Ann Arbor Stage (III-IV)	**25 (92.6%)**
MIPI: Low / Intermediate / High Risk	**6 (22.2%) / 11 (40.7%) / 10 (37.0%)**
Ki-67: < 30% / ≥30% / Not available	**15 (55.6%) / 10 (37.0%) / 2 (7.4%)**
Histology and Genetics	
Classical / Blastoid / Other Variant	**19 (70.4%) / 3 (11.1%) / 5 (18.5%)**
TP53 Status (Negative WT / Positivo)	**19 (70.4%) / 3 (11.1%)***

**Note: TP53 status not evaluated or indeterminate in 5 patients (18.5%).*

ECOG: Eastern Cooperative Oncology Group; Ki-67: cell proliferation marker antigen; MIPI: Mantle Cell Lymphoma International Prognostic Index; WT: Wild-type.

Adverse Event / Tolerability	Induction (n=27)	Maintenance (n=23)
Most Frequent Adverse Events, n (%)		
Infections	**8 (29%)**	3 (13%)
Hematological (Neutropenia ≥3)	**7 (25%)**	3 (13%)
Hemorrhagic	1 (3.7%)	**3 (13%)**
Cardiovascular (AF / HTN)	1 (3.7%) AF	**3 (13%)** HTN
Gastrointestinal	0 (0%)	2 (8.6%)
Impact on Ibrutinib Dose, n (%)		
Delay / Temporary interruption	4 (14%)	**4 (17.4%)**
Dose reduction (to 420 mg)	0 (0%)	**4 (17.4%)**
Definitive discontinuation (due to AE)	0 (0%)	0 (0%)*

**Note: 1 patient (4.3%) discontinued due to disease progression, not toxicity.*

AF: Atrial Fibrillation; HTN: Hypertension; AE: Adverse Event.

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